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EXAMINER

DEVI, SARVAMANGALA J N

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18

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No. 09/359,426	Applicant(s) Cripps et al.
Examiner S. Devi, Ph.D.	Art Unit 1645

— The MAILING DATE of this communication appears on the cover sheet with the correspondence address —

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on Jan 14, 2002

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-35 is/are pending in the application.

4a) Of the above, claim(s) 10-17 and 28-35 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-9 and 18-27 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some* c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. _____.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892)

4) Interview Summary (PTO-413) Paper No(s). _____

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

5) Notice of Informal Patent Application (PTO-152)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4.

6) Other: _____

DETAILED ACTION

Preliminary Amendments

1) Acknowledgment is made of Applicants' preliminary amendments filed 07/19/00, 12/11/00 and 01/14/02 (paper no. 6, 9 and 17). With these, Applicants have amended the specification.

Election

2) Acknowledgment is made of Applicants' election, without traverse, of invention I, claims 1-9 and 18-27, filed 07/19/00 (paper no. 6) in response to the restriction requirement mailed 05/19/00 (paper no. 5).

Status of Claims

3) Claims 1-35 are pending.

Claims 2 and 3 have been amended via the amendment filed 12/11/00.

Claim 5 has been amended via the amendment filed 01/14/02.

Claims 10-17 have been withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.

Claims 1-9 and 18-27 have been elected via the election filed 07/19/00 and are under examination. An Action on the Merits for this claim is issued.

Information Disclosure Statement

4) Acknowledgment is made of Applicants' Information Disclosure Statement filed 11/03/99 (paper no. 4). The information referred to therein has been considered and a signed copy is attached to this Office Action (paper no. 18).

Sequence Listing

5) Acknowledgment is made of Applicants' raw sequence listing filed 07/23/01 (paper no. 14) which has been entered on 07/31/01 (paper no. 15).

Priority

6) This application is a Continuation-in-part application of PCT/GB98/00217, filed 26 January 1998, which claims priority to application 9701489.8, filed 24 January 1997 filed in Great Britain. It is noted that Applicants have submitted a certified copy of the priority document, 9701489.8.

Drawings

7) The drawing submitted in the instant application is not objected to by the Draftsperson under 37 C.F.R 1.84 or 1.152 and as such, the drawing has been approved as formal drawing.

Specification - Informalities

8) The specification is objected to for the following reasons:

(i) The instant application is informal in the format or arrangement of the specification. The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the Applicants' use.

Content of Specification

- (a) Title of the Invention: See 37 C.F.R 1.72(a). The title of the invention should be placed at the top of the first page of the specification. It should be brief but technically accurate and descriptive, preferably from two to seven words.
- (b) Cross-References to Related Applications: See 37 C.F.R 1.78 and M.P.E.P § 201.11.
- (c) Statement Regarding Federally Sponsored Research and Development: See M.P.E.P § 310.
- (d) Reference to a "Microfiche Appendix": See 37 C.F.R 1.96(c) and M.P.E.P § 608.05. The total number of microfiche and the total number frames should be specified.
- (e) Background of the Invention: The specification should set forth the Background of the Invention in two parts:
 - (1) Field of the Invention: A statement of the field of art to which the invention pertains. This statement may include a paraphrasing of the applicable U.S. patent classification definitions of the subject matter of the claimed invention. This item may also be titled "Technical Field."
 - (2) Description of the Related Art: A description of the related art known to the applicant and including, if applicable, references to specific related art and problems involved in the prior art which are solved by the applicant's invention. This item may also be titled "Background Art."

(f) Brief Summary of the Invention: A brief summary or general statement of the invention as set forth in 37 C.F.R 1.73. The summary is separate and distinct from the abstract and is directed toward the invention rather than the disclosure as a whole. The summary may point out the advantages of the invention or how it solves problems previously existent in the prior art (and preferably indicated in the Background of the Invention). In chemical cases it should point out in general terms the utility of the invention. If possible, the nature and gist of the invention or the inventive concept should be set forth. Objects of the invention should be treated briefly and only to the extent that they contribute to an understanding of the invention.

(g) Brief Description of the Several Views of the Drawing(s): A reference to and brief description of the drawing(s) as set forth in 37 C.F.R 1.74.

(h) Detailed Description of the Invention: A description of the preferred embodiment(s) of the invention as required in 37 C.F.R 1.71. The description should be as short and specific as is necessary to describe the invention adequately and accurately. This item may also be titled "Best Mode for Carrying Out the Invention." Where elements or groups of elements, compounds, and processes, which are conventional and generally widely known in the field of the invention described and their exact nature or type is not necessary for an understanding and use of the invention by a person skilled in the art, they should not be described in detail. However, where particularly complicated subject matter is involved or where the elements, compounds, or processes may not be commonly or widely known in the field, the specification should refer to another patent or readily available publication which adequately describes the subject matter.

(i) Claim or Claims: See 37 C.F.R 1.75 and M.P.E.P § 608.01(m). The claim or claims must commence on separate sheet. (37 C.F.R 1.52(b)). Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation. There may be plural indentations to further segregate subcombinations or related steps.

(j) Abstract of the Disclosure: A brief narrative of the disclosure as a whole in a single paragraph of 250 words or less on a separate sheet following the claims.

(k) Drawings: See 37 C.F.R 1.81, 1.83-1.85, and M.P.E.P § 608.02.

(l) Sequence Listing: See 37 C.F.R 1.821-1.825.

The instant specification is further objected to because of the reasons given below:

(ii) The use of the trademarks has been noted in this application. For example, see page 10, line 12: "Tween-20"; page 10, line 10: "tween 20"; page 5, lines 19 and 20: "zwittergent 3-14"; and page 6, line 7: "Prep Cell". The recitations should be capitalized wherever they appears and be accompanied by the generic terminology. Each letter of the trademark must be capitalized. See M.P.E.P 608.01(V) and Appendix I. Although the use of trademarks is permissible in patent applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. It is suggested that Applicants examine the whole specification to make similar corrections to the trademarks, wherever such recitations appear.

(iii) The composition of amino acid sequences, SEQ ID NO: 1 and SEQ ID NO: 2, recited on page 7 of the specification and in the instant claims is inconsistent. While page 7 of the specification recites "?" in certain positions of these two sequences, claims 2 and 4 recite "Xaa" in these positions. It is not clear what "?" stands for.

(iv) The name(s) of bacterial species in certain part(s) of the instant specification is not italicized. See for example, page 15, line 24: "P. aeruginosa". To be consistent with the practice in the art, the names of all bacterial species in the instant disclosure be italicized throughout the specification.

Rejection(s) under 35 U.S.C. § 101

9) Claims 1-9 are rejected under 35 U.S.C. § 101, as being directed to a non-statutory subject matter. Claims 1 and 3-6 encompass a protein antigen from *P. aeruginosa* or an antigenic fragment thereof, and therefore reads on products of nature, i.e., naturally occurring antigen. The claims lack limitations which distinguish the products from those that may exist naturally. Consequently, the claims do not embody patentable subject matter as defined in 35 U.S.C § 101. See MPEP 2105. It is suggested that Applicants use limitations, such as, --An

isolated--, --A purified--, or --An isolated and purified-- in connection with the outer membrane protein antigen in connection with the products to reflect the hands of the inventors in the production or creation of the claimed product as is supported in the specification on page 6, line 13 and page 10, line 8.

Rejection(s) under 35 U.S.C. § 112, First Paragraph

10) Claims 2, 3, 5, 6, 8, 18, 22, 23, 25 and 26 are rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are viewed as not providing sufficient and/or clear written description under 35 U.S.C § 112, first paragraph, for one to practice the invention as claimed.

The full structural composition of the recited N-terminal sequences of the claimed protein having the amino acid sequences of SEQ ID NO: 1 and SEQ ID NO: 2 is critical or essential to make and use the claimed protein and an antigenic fragment thereof, which are meant for use as a diagnostic or immunogenic vaccine composition. However, the instant specification and the claims lack adequate written description with regard to the full structural composition of the N-terminal sequence of the protein. There is lack of written description as to which specific fragment of the claimed protein or of the amino acid sequence of SEQ ID NO: 1 or 2 is encompassed in the claimed antigenic fragment. The specification lacks written description as to whether retention of any fragment from any part of the claimed protein or of SEQ ID NO: 1 or 2 (i.e., terminal or central parts) would yield a protein fragment that would have the expected biologic, i.e., antigenic and immunogenic or vaccine functions. Without a clear and precise description of which amino acid residues are present in which position of the recited N-terminal sequence of the claimed protein, one cannot reproducibly practice the invention as claimed, without undue experimentation. The instant specification, as originally filed, does not identify the full amino acid sequence of the N-terminal sequence of the claimed protein or a fragment thereof that possesses antigenic or immunogenic properties, without which one of ordinary skill in the art cannot practice the invention as currently claimed. It should be noted that *Vas-Cath Inc. v. Mathukar*, 19 USPQ2d 1111 states that Applicant "must convey with reasonable clarity to

those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, is for purposes of the ‘written description’ inquiry, whatever is now claimed.” See page 1117. The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” See page 1116 of *Vas-Cath Inc. V. Mathukar*, 19 USPQ2d 1111. Applicants should also note that *Vas-Cath Inc. V. Mathukar*, 19 USPQ2d 1111 makes clear that the written description provision of 35 U.S.C § 112, first paragraph, is severable from its enablement provision. See page 1115. Irrespective of the simplicity or complexity of the isolation method, conception is not achieved until reduction to practice has occurred. Adequate written description requires more than a mere statement that it is a part of the invention. The claimed product having the recited N-terminal sequence and the function(s) is required. Therefore, the claims are viewed as not meeting the written description provision of 35 U.S.C § 112, first paragraph.

11) Claims 2, 3, 5, 6, 8, 18, 22, 23, 25 and 26 are rejected under 35 U.S.C § 112, first paragraph, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are viewed as not meeting the enablement provisions of 35 U.S.C § 112, first paragraph, for one of ordinary skill in the art to practice the invention.

Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

In the instant case, one or more of the instant claims encompass a protein antigen of *P. aeruginosa* having a molecular weight in the range of about 60 to about 65 kDa by SDS-PAGE and an N-terminal sequence of SEQ ID NO: 1 or 2 as recited in claim 2, 3 or 5. The specification

on page 2 recites SEQ ID NO: 1 and 2. These sequences are 19 amino acid residues-long and contain 11 and 3 unknown amino acid residues respectively which are designated as “?”. There is no written description as to what amino acid residue each “?” stands for. Whether or not each ? represents the same or different amino acid residue, conservative or non-conservative amino acid residues etc., is unknown or undisclosed. Several amino acid residues in the N-terminal sequence are indicated to be ‘probable’ or ‘possible’ on page 7 of the specification. Even after guessing the probable amino acid residues, 11 amino acid residues in SEQ ID NO: 1 and 3 amino acid residues in SEQ ID NO: 2 remain as “?” residues. In the absence of the precise structural composition of the amino acid sequence of SEQ ID NO: 1 and SEQ ID NO: 2, one cannot make and use the claimed protein antigen or an antigenic fragment thereof. There is no guarantee that such an amino acid sequence or a fragment thereof would retain the desired antigenic properties and serve to be a diagnostic or a immunogenic vaccine composition. The art reflects functional unpredictability with regard to this. It is well known in the absence or deletion of, or the substitution of a single amino acid residue in a protein or a polypeptide can dramatically change or eliminate the function(s) of that protein or polypeptide and render it non-antigenic or antigenically non-specific. The specification, as originally filed, does not provide enablement and/or specific guidance to one of ordinary skill in the art as to how to obtain, for example, an antigenic fragment claimed in claim 6, which is a fragment of the protein claimed in claim 3 that contains SEQ ID NO: 2. In the absence of the concise structural composition of such an antigenic fragment, one cannot practice the invention as claimed without undue experimentation. A full disclosure of the amino acid sequence of SEQ ID NO: 1 and SEQ ID NO: 2 is critical since a skilled artisan can not predict the exact amino acid residue that should be present in positions now indicated as “?” or “Xaa”. The art reflects sensitivity of proteins to alterations of even a single amino acid in a sequence. For instance, Burgess *et al* (*J. Cell Biol.* 111: 2129-2138, 1990) teach that replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Similar teachings are provided by Lazar *et al* (*Mol. Cellular Biol.* 1988, 8: 1247-1252) who show that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity, while

replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. Therefore, without a full disclosure of all the amino acid residues contained within the amino acid sequences of SEQ ID NO: 1 and SEQ ID NO: 2, or a fragment thereof, one of ordinary skill in the art cannot be sure of the sequences embraced by the claims and would not be able to make and use these protein sequences or their fragments as recited in the instant claims, without undue experimentation. One of ordinary skill in the art would not be able to make and use such protein sequences or fragments, for example, as a component of a vaccine or immunogenic composition or diagnostic antigen, without undue experimentation.

Neither the specification, as originally filed, nor the art at the time of the claimed invention, taught that the claimed protein fragment would serve as a vaccine capable of providing protection to a host. The specification fails to disclose that the claimed protein fragment serves as a diagnostic reagent in a kit, or as a vaccine capable of reducing morbidity and/or mortality of the disease caused by *Ps. aeruginosa*. The specification must be enabling at the time the invention was made; developments after the time of filing are of no consequence to what one skilled in the art would have believed at the time of filing. *See In re Wright*, 27 USPQ2d 1510. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. *See Genentech Inc. v. Novo Nordisk A/S Ltd.*, 42 USPQ2d 1001. There is no predictability that any fragment of a bacterial protein would serve as an antigen being capable of binding to specific antibodies. For instance, the state of the art on bacterial polypeptides, for example, demonstrates unpredictability associated with the presence of an epitope on any fragment from any part of a given bacterial polypeptide antigen. For example, McGuinness *et al.* (WO 90/06696) clearly demonstrate that portions of a bacterial polypeptide comprising ten contiguous amino acid residues from any random part(s) of the whole polypeptide molecule do not contain the antigenic epitope(s) that is recognized by bactericidal (protective) antibodies (see entire document, especially Figure 5). Every 10-mer portion on this bacterial polypeptide did not contain such epitope(s) indicating that the prophylactic (protective) or therapeutic efficacy of any fragment from any portion of a bacterial polypeptide antigen is not predictable. Therefore, a fragment from any portion of the instantly claimed protein cannot be assumed to contain or retain antigenic determinants that are

needed for antigenicity, immunogenicity, or that induce prophylactic or therapeutic immune responses. Clearly, the specification does not teach protein fragments that contain an antigenic epitope. Since which fragment would retain the antigenic specificity is neither disclosed, nor could be predicted, one of ordinary skill would be forced into experimentation that is undue. Without a disclosure of the specific amino acid residues contained within the recited N-terminal sequence or a fragment thereof, one of ordinary skill in the art cannot be sure of the amino acid or nucleotide sequences embraced by the claims and would not be able to make and use the nucleic acid sequence(s) as recited in the instant claims, without undue experimentation. One of ordinary skill in the art would not be able to make and use such amino acid sequences, for example, as prophylactic, therapeutic or a diagnostic reagents, because there is no disclosure as to what amino acid residues are embraced by the claims. The claims are viewed as not meeting the enablement provisions of 35 U.S.C § 112, first paragraph.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

12) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

13) Claims 2, 4-8, 18, 19 and 21-27 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claims 4 and 6 lack proper antecedent basis for the recitation “the protein defined in claim...”. Claim 4 depends from claim 1, and claim 6 depends from claim 3. Claims 1 and 3 recite “a protein antigen”, but not a “protein”. For clarity and proper antecedent basis, it is suggested that Applicants replace the recitation with --the protein antigen according to claim...--.

(b) Claims 2, 4, 6, 7, 18 and 21 lack proper antecedent basis for the recitation “the protein claim ...”. The instant claims depend directly or indirectly from claim 1 or 3, which recites a “protein antigen”, as opposed to a ‘protein’.

(c) Claims 5, 8, 19, 22, 23, 25 and 26, which depend from claim 4, 6 or 21, are also rejected under 35 U.S.C § 112, second paragraph, as being indefinite, because of the indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 102

14) The following is a quotation of the appropriate paragraph(s) of 35 U.S.C. § 102 that form the basis for the rejection(s) under this section made in this Office action:

A person shall be entitled to a patent unless –
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15) Claims 1, 7, 21 and 24 are rejected under 35 U.S.C § 102(b) as being anticipated by Yamano *et al.* (*J. Antimicrob. Chemother.* 26: 175-184, 1990), or Yoshinori *et al.* (*Appl. Microbiol. Biotechnol.* 40: 892-897, 1994), or Brown *et al.* (*J. Bacteriol.* 177: 6536-6544, 1995), or Yamaguchi *et al.* (*Jpn. J. Bacteriol.* 41: 701-708, 1986), or Sompolinsky *et al.* (*Acta Pathol. Microbiol. Scand. Sect. B* 88: 143-149, 1980), or Barhaila *et al.* (*FEMS Microbiol. Lett.* 51: 169-172, 1988), or Meyer *et al.* (*Mol. Microbiol.* 4: 1401-1405, 1990), or Fernandes *et al.* (*Infect. Immun.* 33: 527-32, 1981).

The limitation “vaccine” is viewed as an intended use of the claimed protein antigen and is therefore viewed as not having any patentable weight.

Yamano *et al.* teach the protein C of *Ps. aeruginosa* which has a molecular weight of 66K (i.e., 66,000 kDa) as measured by SDS-PAGE (see Figure 1; and pages 180 and 181).

Yoshinori *et al.* teach an outer membrane protein antigen of *Ps. aeruginosa* having a molecular weight of 66 kDa (Figure 2 and 5; and page 896).

Brown *et al.* teach a purified *Ps. aeruginosa* catalase protein having a molecular weight of 57,127 (i.e., about 60 kDa) as measured by SDS PAGE (see abstract; page 6541, right column; page 6537, right column; and Figure 5B).

Yamaguchi *et al.* teach a major outer membrane protein of *Ps. aeruginosa* having a molecular weight of 60 kilodaltons as measured by SDS-PAGE (see abstract).

Sompolinsky *et al.* teach a purified protein antigen of *Ps. aeruginosa* having a molecular weight in the range of 59 - 62000 and 62-65000 as measured by SDS-PAGE (see abstract; Figure 3; and pages 147 and 148).

Barhaila *et al.* teach an outer membrane protein of *Ps. aeruginosa* having a molecular weight of approximately 60,000 as measured by SDS-PAGE (see summary; see page 171; and Figures 2 and 3).

Meyer *et al.* teach an outer membrane protein of *Ps. aeruginosa* having a molecular weight in the range of 60-65 kD as measured by SDS-PAGE (see page 1402; and Figure 1).

Fernandes *et al.* teach a purified *Ps. aeruginosa* outer membrane protein having a molecular weight of 58,500 (i.e., about 60 kDa) as measured by SDS PAGE (see abstract; page 528, right column; page 529; Figures 2 and 3; and page 531, left column). The protein was immunogenic (see abstract).

Although the prior art references may not expressly disclose the *Ps. aeruginosa* to be antigenic, a protein having a size of larger than 50,000 molecular weight would inherently serve as an antigenic or immunogenic composition and would elicit an immune response in a subject.

Claims 1, 7, 21 and 24 are anticipated by Yamano *et al.* or Yoshinori *et al.* or Brown *et al.* or Yamaguchi *et al.* or Sompolinsky *et al.* or Barbhaiya *et al.* or Meyer *et al.* or Fernandes *et al.*

16) Claims 1, 7 and 9 are rejected under 35 U.S.C § 102(b) as being anticipated by Yamano *et al.* (*J. Antimicrob. Chemother.* 26: 175-184, 1990), or Yoshinori *et al.* (*Appl. Microbiol. Biotechnol.* 40: 892-897, 1994), or Yamaguchi *et al.* (*Jpn. J. Bacteriol.* 41: 701-708, 1986), or Barbhaiya *et al.* (*FEMS Microbiol. Lett.* 51: 169-172, 1988), or Meyer *et al.* (*Mol. Microbiol.* 4: 1401-1405, 1990).

Yamano *et al.* teach the protein C of *Ps. aeruginosa* which has a molecular weight of 66K (i.e., 66,000 kDa) as measured by SDS-PAGE (see Figure 1; and pages 180 and 181).

Yoshinori *et al.* teach an outer membrane protein antigen of *Ps. aeruginosa* having a molecular weight of 66 kDa (Figure 2 and 5; and page 896).

Yamaguchi *et al.* teach a major outer membrane protein of *Ps. aeruginosa* having a molecular weight of 60 kilodaltons as measured by SDS-PAGE (see abstract; Figures 4 and 5).

Barbhaiya *et al.* teach an outer membrane protein of *Ps. aeruginosa* having a molecular weight of approximately 60,000 as measured by SDS-PAGE (see summary; see page 171; and Figures 2 and 3).

Meyer *et al.* teach an outer membrane protein of *Ps. aeruginosa* having a molecular weight in the range of 60-65 kD as measured by SDS-PAGE (see page 1402; and Figure 1).

Although the prior art references may not expressly disclose their *Ps. aeruginosa* protein

antigen composition to be further comprising one or more *Ps. aeruginosa* antigens, since the prior art protein antigens are not fully purified preparations, these antigens would inherently contain additional antigens of *Ps. aeruginosa*.

Claims 1, 7 and 9 are anticipated by Yamano *et al.*, or Yoshinori *et al.*, or Yamaguchi *et al.*, or Barbhaiya *et al.*, or Meyer *et al.*

17) Claims 1 and 4 are rejected under 35 U.S.C § 102(b) as being anticipated by Sipos *et al.* (*Infect. Immun.* 59: 3219-3226, 1991).

Sipos *et al.* teach a 60 kDa protein antigen of *Ps. aeruginosa* and a decapeptide antigenic fragment of the same (see abstract).

Claims 1 and 4 are anticipated by Sipos *et al.*

18) Claims 1, 4, 21 and 24 are rejected under 35 U.S.C § 102(b) as being anticipated by Hancock *et al.* (WO 93/24636).

Hancock *et al.* teach an outer membrane protein of *Ps. aeruginosa* having a molecular weight of about 65 kDa as measured by SDS PAGE and an oligopeptide or a fragment thereof, which have use as diagnostics and vaccines. The protein or the antigenic peptide could give rise to an immune response in immunized animals which protects against infection (see Figure 3; paragraph bridging pages 15 and 16; pages 16, 18 and 22).

Claims 1, 4, 21 and 24 are anticipated by Hancock *et al.*

Rejection(s) under 35 U.S.C. § 103

19) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

20) Claims 1, 7, 19-21, 24 and 27 are rejected under 35 U.S.C § 103(a) as being unpatentable over Yamano *et al.* (*J. Antimicrob. Chemother.* 26: 175-184, 1990), or Yoshinori *et al.* (*Appl. Microbiol. Biotechnol.* 40: 892-897, 1994), or Brown *et al.* (*J. Bacteriol.* 177: 6536-6544, 1995), or Yamaguchi *et al.* (*Jpn. J. Bacteriol.* 41: 701-708, 1986), or Sompolinsky *et al.* (*Acta Pathol. Microbiol. Scand. Sect. B* 88: 143-149, 1980), or Barhaiya *et al.* (*FEMS Microbiol. Lett.* 51: 169-172, 1988), or Meyer *et al.* (*Mol. Microbiol.* 4: 1401-1405, 1990), or Fernandes *et al.* (*Infect. Immun.* 33: 527-32, 1981), or Hancock *et al.* (WO 93/24636), or Sipos *et al.* (*Infect. Immun.* 59: 3219-3226, 1991).

The teachings of Yamano *et al.*, Yoshinori *et al.*, Brown *et al.*, Yamaguchi *et al.*, Sompolinsky *et al.*, Barhaiya *et al.*, Meyer *et al.*, Fernandes *et al.*, Hancock *et al.* or Sipos *et al.* are explained above, which do not expressly teach their protein antigen being present in a kit, or being present with an adjuvant.

However, methods of assembling a diagnostic kit using an art-disclosed protein product, or adding a conventional adjuvant to an art-disclosed protein product is well known and routinely practiced in the art, and therefore, would have been *prima facie* obvious to a skilled artisan at the time the invention was made to produce such a diagnostic kit for *in vitro* diagnosis of *Ps. aeruginosa* infection using the protein product of the prior art, or such a composition by adding an art-known adjuvant to the protein product of the prior art. A skilled artisan would have been motivated to produce the instant invention for the expected benefit of making readily available the prior art protein antigen, or for commercializing the prior art protein antigen beneficially for diagnostic or therapeutic use.

Claims 1, 7, 19-21, 24 and 27 are *prima facie* obvious over the prior art of record.

Objection(s)

21) Claims 1, 3, 18 and 19 are objected to for the following reasons:
(a) Claims 1 and 3 are objected to for reciting “60kDa” and “65kDa” without leaving a space in between. It is suggested that Applicants replace the recitations with --60 kDa-- and --

65 kDa— respectively.

(b) Claims 18 and 19 are objected to for the recitation “in the detecting” (see line 1). To be consistent with the claim language used in claim 20, it is suggested that Applicants replace the recitation with --in detecting--.

Relevant Prior Art

22) The prior art made of record and not currently relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

- Kukor *et al.* (*J. Bacteriol.* 170: 4458-4465, 1988) teach the cloning and expression of the catA gene of *Ps. aeruginosa* (see entire document).
- Nurizzo *et al.* (*Structure* 5: 1157-1171, 1997) teach two 60 kDa catalyzing enzymes of *Ps. aeruginosa* (see abstract).

Remarks

23) Claims 1-9 and 18-27 stand rejected.

24) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242, which is able to receive transmissions 24 hours a day and 7 days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

25) Any inquiry concerning this communication or earlier communication(s) from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. A message may be left on the Examiner's voice mail service. The Examiner can normally be reached on Monday to Friday from 7.15 a.m to 4.15 p.m. except one day each bi-week which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

July, 2002

S. DEVI, PH.D.
PRIMARY EXAMINER